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# Ventricular noncompaction: Over or under diagnosis?

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## KEYWORDS

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**Abstract** Ventricular noncompaction (VNC) describes a cardiomyopathy characterized by excessive myocardial trabeculations and deep intertrabecular recesses. Detection rates are increasingly rising and the frequency of NVC has changed from a disease that is thought to be rare to that described as 'relatively common'. However, there had been a number of un-answered questions regarding the clinical and echocardiographic features of VNC. In this review we discuss the frequency of VNC and emphasize its distinctive clinical features and associations.

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## 1. Introduction

Ventricular noncompaction (VNC) describes a primary genetic cardiomyopathy that has recently intensively investigated and is characterized by excessive myocardial trabeculations and deep inter trabecular recesses (Hare, 2008). It has a variable clinical picture heart failure due to myocardial dysfunction being the most common presenting feature and thrombo-embolism, arrhythmias and sudden death are known complications (Ali and Godman, 2004; Oechslin et al., 2000). Detection rates are increasingly rising and the reported frequency of NVC has changed a disease that is thought to one described as 'relatively common' (Pignatelli et al., 2003). There remain a number of un-answered questions regarding VNC:

What is its echocardiographic definition?  
What is its frequency? Is it over or under diagnosed?  
Is it a primary problem or secondary to pressure/volume overload?  
What are the distinctive clinical and echocardiographic features/associations?

## 2. What is the echocardiographic definition of VNC?

Echocardiography done for large numbers of individuals with normal hearts screened for different reasons have shown that trabeculations of variable number and location can be present (Veglia et al., 2004). The appearance of VNC on echocardiograms of otherwise normal asymptomatic patients in middle age may indicate that VNC can exist for many years without causing any problems. Moreover, postmortem study of the left ventricle myocardium, of apparently normal hearts showed that prominent left ventricular trabeculations were common variants of the normal human heart. Their size, shape and location may lead to their being misinterpreted as mural thrombi or cardiomyopathy (Edwards et al., 1987).

Although these studies indicate that trabeculations can exist in normal hearts the definition of VNC involves more than the presence of trabeculations and there must be other features to

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diagnose this entity. Many echocardiographic criteria have been postulated to diagnose VNC, the most widely used diagnostic criteria can be summarized as: (1) appearance of at least four prominent trabeculations and deep intertrabecular recesses; (2) appearance of blood flow from the ventricular cavity into the intertrabecular recesses as visualized by color Doppler imaging; (3) the segments of noncompacted myocardium mainly involve the apex and the inferior mid and lateral parts of the left ventricular wall and typically show a two-layered structure with an end systolic ratio greater than two between the noncompacted subendocardial layer and the compacted subepicardial layer; and (4) absence of coexisting cardiac abnormalities (Yelbuz et al., 2007).

Although many authors require the exclusion of associated cardiac abnormalities to define VNC, we as well as others (Hare, 2008; Ozkutlu et al., 2002) have used the above criteria in patients with VNC associated with complex and noncomplex congenital heart disease. The ratio of noncompacted to compacted layers of 2 or more is rather arbitrary and some authors had used an even lower ratio of  $>1.4:1$  which can result in over diagnosis of this entity (Pignatelli et al., 2003). VNC have been described in the right ventricle (Ozkutlu et al., 2002; Burke et al., 2005) which is normally more trabeculated than the left. This can cause some confusion and be a potential for over diagnosis, but we believe that the pattern of normal right ventricle trabeculation and its distribution in the septal surface can be distinguished from the more bizarre pattern of VNC which tends to involve the apical segments.

### 3. What is the true frequency? Is it over or under diagnosed?

Epidemiological studies from Australia revealed a frequency of VNC of 9% of all childhood cardiomyopathies, the highest among unclassified cardiomyopathies (Nugent et al., 2003). In the United States of America Pignatelli et al. found a similar frequency of VNC in patients with cardiomyopathy and concluded that the entity is relatively common (Pignatelli et al., 2003).

A recent study in UK had shown that the frequency of VNC is 3% among newly diagnosed cases of childhood cardiomyopathy (Andrews et al., 2008).

A much higher frequency of 23% was found by Kohli et al. in a cohort of patients with impaired myocardial function which they considered reflected that this disease is underestimated. However, the same authors found that echocardiographic criteria for VNC were positive in eight normal controls which could indicate over sensitivity of the criteria (Kohli et al., 2008). On the other hand this finding could indicate that the prevalence of VNC in the general population is more than expected. This theory is supported by finding of asymptomatic individuals with features of VNC on echocardiograms done as screening for different reasons (e.g. patients with Down's syndrome) as well as asymptomatic family members of patients with VNC (Hare, 2008; Murphy et al., 2005).

We believe that VNC is underdiagnosed and overlooked by echocardiographers. In our experience and also other authors many patients were missed on initial echocardiograms. A histopathological study on 14 paediatric hearts with VNC for patients who died because of sudden unexpected death and heart failure found that the diagnosis was suspected before death in only one patient (Burke et al., 2005) and this strongly supports our belief that this disease is underdiagnosed. The true inci-

dence of this abnormality cannot be extrapolated from hospital studies and can only be determined from large population based echocardiographic screening.

### 4. Is it a primary problem or secondary to pressure/volume overload?

Some authors have suggested that VNC could be a response of the myocardium to abnormal loading conditions like pressure or volume overload (Stollberger and Finsterer, 2004). This may seem true, in fact in our own practice we have seen some patients with volume overload (large ventricular septal defect and mitral valve regurgitation due to rheumatic heart disease) and pressure overload (coarctation of the aorta and subaortic stenosis) who have VNC. However, this myocardial 'reaction' occurs only in certain patients and the majority of patients with similar lesions react by simple dilatation or hypertrophy without the appearance of VNC. Therefore, these patients with VNC have got an intrinsic problem in their myocardium that causes this unusual reaction. In addition some patients with VNC manifest the abnormal myocardium without any underlying volume or pressure overload. We do believe that this entity is a primary myocardial deformity, the phenotypic expression can be a continuum with mild forms falling into the 'normal' that predisposes to the known complications of myocardial dysfunction, arrhythmias and thrombo-embolism rather than a secondary response to abnormal loading conditions. We agree with the opinion of McKenna et al. that the extent of ventricular compaction may be a continuous trait within the population, more subtle forms are well tolerated in the presence of normal loading conditions and identified only by routine screening. On the other hand more severe forms present with the known complications of myocardial dysfunction, arrhythmias and thrombo-embolism (Srijta and McKenna, 2008).

### 5. What are the distinctive clinical and echocardiographic features/associations?

In a review of 52 patients with VNC from Saudi Arabia and Sudan we noted important and unique features for this disease (Sulafa, 2008a):

1. Female preponderance: In isolated forms of VNC and those associated with mitral valve disease (see below) we observed that the female to male ratio is 4:1 and 6:1, respectively. This ratio stands in sharp contrast to the Western literature where most studies showed a male dominance (Pignatelli et al., 2003; Nugent et al., 2003).
2. Association with mitral regurgitation: In 2004 we described a new association between VNC and mitral regurgitation in four patients (2 months, 6 months, 18 months and 2 years) associated with specific mitral valve changes (superior coaptation and a zigzag deformity of the anterior mitral leaflet) and significant mitral regurgitation (Ali et al., 2004). One infant had a normal mitral valve and VNC at 2 months of age then developed mitral regurgitation later in infancy. Then we reported six more patients with this association at different ages (Sulafa, 2008b, in press). All 10 patients exhibit similar characteristic mitral valve changes (Fig. 1). The etiology of mitral regurgitation in



**Figure 1** Four chamber view showing deformity of the anterior mitral leaflet, thickening of both anterior and posterior leaflets and dilated left atrium.

these patients is not clear but cannot be explained by congenital or known acquired causes of mitral regurgitation. Interestingly, a histopathological study from children with VNC had shown an associated polyvalvar dysplasia involving the mitral valve and this finding supports our belief that NVM/mitral regurgitation is a distinct association that needs to be looked for (Burke et al., 2005).

3. Relapsing VNC: We as well as others described the relapsing and remitting course of VNC in different age groups (Hare, 2008; Pignatelli et al., 2003; Menon et al., 2007). In our cohort patients had two short relapses followed by long remissions while other authors described a transient period of improvement followed by later deterioration. One patient had two short episodes of heart failure followed by long remissions: a 15-year-old Sudanese girl who initially had heart failure at 7 years of age and needed



**Figure 2** Short axis view showing a large thrombus (arrow) in the left ventricle apex and noncompacted left ventricle myocardium.

hospitalization. She improved on diuretics and then remained well without medications till 15 of age when she presented to us with severe myocardial dysfunction and left ventricle thrombus (Fig. 2). She experienced a cerebrovascular accident with left sided hemiparesis that resolved after 5 days on anticoagulation therapy. Her ejection fraction improved over 2 weeks with complete resolution of symptoms. Echocardiography continued to show the myocardial trabeculations and recessions. This relapsing course is a unique feature of VNC that can be the only clinical manifestation that distinguishes VNC from other types of cardiomyopathy.

In conclusion, we believe that VNC is a relatively common primary cardiomyopathy with distinct echocardiographic characteristics that is often under diagnosed. Careful application of diagnostic criteria helps to minimize over diagnosis.

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